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TITLE: Tritherapy (Spinalon)-Elicited Spinal Locomotor Network Activation : Phase I-IIa  
Clinical Trial in Spinal Cord-Injured Patients.

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14. ABSTRACT . This study aims to assess safety and preliminary efficacy of a first-in-class drug treatment called SPINALON that is designed to acutely trigger episodes of automatic walking in chronic spinal cord-injured patients.  It is a single administration, dose escalation, randomized, controlled, and double-blind study which main objective is to determine safety, tolerability and maximum tolerated dose of SPINALON. As a secondary objective, evidence of efficacy (Central Pattern Generator activation and corresponding rhythmic and locomotor-like movement induction) will be sought.  The clinical utility of this treatment is to allow correspondingly elicited-regular treadmill training (e.g., active physical activity induced three times per a week) to become a holistic solution for the prevention, reversal or reduction of metabolic and systemic health problems and deregulation (skeletal muscle and bone, cardiovascular, hormonal, immune, neuronal systems) typically found in chronic spinal cord-injured patients					
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## SECTION 1

### **Brief introduction:**

This study aims to assess safety and preliminary efficacy of a first-in-class drug treatment called SPINALON that is designed to acutely trigger episodes of automatic walking in chronic spinal cord-injured patients.

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## SECTION II

### Description of progress:

#### a) Overall:

The project started officially on September 30<sup>th</sup>, 2011. We immediately began the preparation and submission of the corresponding documents to Health Canada and McGill University Health Center (MUHC) for Canadian regulatory approval (IND/CTA) and Ethics Review Board (ERB) approval. Approval from Health Canada (tasks 1a-1d completed) has been granted during the first three months (see the previous quarterly report). We then obtained approval in May of the institution (Montreal General Hospital/McGill University Health Center) where all the study will be conducted (task 1e). We subsequently prepared the final documents to be sent to CDMRP/HRPO ERB review board (task 1f) for review and approval (sent May 30<sup>th</sup>). Upon analysis of these documents by Mrs Melanie Frank, we received on July 31<sup>th</sup> 2012 a list of significant changes to be made including new personnel to hire (e.g., a study monitor for AEs monitoring/reporting as well as a Clinical Trial Associated for data monitoring). Corresponding answers and updated/corrected versions of our documents were submitted to Mrs. Frank on October 11<sup>th</sup>, 2012. In parallel, significant corresponding changes needed to be made and were thus proposed for approval (Mrs Iddil Bekirov) on October 9<sup>th</sup>, 2012. However, a few administrative problems have not yet been resolved between the local institution (MUHC – McGill University Health Center) and DOD regarding specific requirements in the contract with Nordic LSP (to allow Dr Prince, Dr Champagne and new CTA to work in MUHC under FWA). In brief, a few problems remain currently under discussion between DOD, MUHC and Nordic LSP. We are waiting for answers from MUHC officials.

#### b) Last three months:

We mainly conducted work aimed to obtain approval from CDMRP ERB (USAMRMC and HRPO):

- **Modifying contract** MUHC-Nordic LSP, study protocol, ICF, and flyer. (See appending documents)
- **Modifying budget** to take into account some of the changed requested by Mrs Frank (e.g., new Study Monitor and CRA) and also task redistribution given that Dr. Barbeau, one of the team members, has abandoned the project for medical reasons.

- **Rebuttal prepared** for Mrs Frank in response to her questions/requested changes (see appending document).

**Prior to the last quarterly period (Sept 2011-June 30 2012):**

- **Review of the Institutional Review Board – MUHC**

**Early May 2012**, we obtained approval from MUHC ERB (part of task 1e).

- **Review by CDMRP/USAMRMC/HRPO**

On **May 30<sup>th</sup> 2012**, we sent all documents required by USAMRM/HRPO for review (part of task 1f). Currently under review (contact: Melanie Frank, [melanie.frank1@us.army.mil](mailto:melanie.frank1@us.army.mil)).

- **Approval from Health Canada (HC) (task 1d)**

Some modifications/clarifications have been done to the protocol and informed consent form based on comments from Health Canada (**task 1c**). On **Nov 23<sup>rd</sup> 2011**, we receive a No Objection Letter (NOL) authorizing Nordic Life Science Pipeline Inc. to conduct the proposed Phase I/IIa study in Canada. A scanned copy of this NOL, is presented on next page (Task 1d).

- **Submission to Health Canada (task 1b)**

120 pages of documentation (e.g., Investigator Brochure, Study Protocol, Informed Consent Form, were submitted to Health Canada Therapeutic Products Directorate (Office of Clinical Trials, 5<sup>th</sup> Floor Holland Cross, Tower B, A/L 3105A, 1600 Scott Street, Ottawa, Ontario, Canada, K1A 0K9) on **October 25<sup>th</sup>, 2011**.

### **SECTION III**

#### **Problems areas:**

##### **a) Current problems:**

As mentioned in the Summary, we are still waiting upon decisions from MUHC regarding an authorization to participate to the study for non-MUHC people/consultants (Dr Champagne as Study Monitor, Dr Prince as EMG monitor, Mr. Fournier as CTA).

##### **b) Anticipated problems:**

The problems described above have led to unexpected delays in the timeline. It has become unclear, even if problems with MUHC are solved shortly, whether or not the project can be entirely completed by March 2014. Six to nine months extra will probably be required.

## SECTION IV

### **Work to be performed next three months:**

Oct-Nov-Dec 2012 – We will attempt to come to a final agreement with MUHC allowing an authorization for all personnel to participate to the project under FWA. Upon this agreement, we will expect approval from the CDMRP/HRPO ERB (**last part of task 1f**).

Upon the latter, resubmission to MUHC ERB of the revised documents need to be made (expedited/level II review process).

Dec 2012/Jan 2013 – First-patient recruitment and initial tests.

## **SECTION V**

### **Administrative comments (optional):**

None